Antimicrobial peptides-loaded smart chitosan hydrogel: release behavior and antibacterial potential against antibiotic resistant clinical isolates

Nourollah Rezaei[1,2], Hatef Ghasemi Hamidabadi[1,2], Sadjad Khosravimelal[3,4,5], Maria Zahiri[6], Zahra Aliakbar Ahovan[7], Maryam Nazm Bojnordi[1,2], Behnaz Sadat Eftekhari[8,9], Ali Hashemi[7], Fatemeh Ganji[3,4], Shahram Darabi[10], Mazaher Gholipourmalekabadi[3,4]*

[1]Immunogenetic Research Center, Department of Anatomy & Cell Biology, Faculty of Medicine, Mazandaran University of Medical Sciences, Sari, Iran
[2]Department of Anatomy & Cell Biology, Faculty of Medicine, Mazandaran University of Medical Sciences, Sari, Iran
[3]Cellular and Molecular Research Centre, Iran University of Medical Sciences, Tehran, Iran
[4]Department of Tissue Engineering & Regenerative Medicine, Faculty of Advanced Technologies in Medicine, Iran University of Medical Sciences, Tehran, Iran
[5]Department of Medical Biotechnology, Faculty of Allied Medicine, Iran University of Medical Sciences, Tehran, Iran
[6]The Persian Gulf Marine Biotechnology Research Center, The Persian Gulf Biomedical Sciences Research Institute, Bushehr University of Medical Sciences, Bushehr, Iran.
[7]Department of Microbiology, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran
[8]Department of Biomedical Engineering, Amirkabir University of Technology, Tehran, Iran.
[9]Department of Physiology and Institute for Medicine and Engineering, University of Pennsylvania, USA.
[10]Cellular and Molecular Research Center, Qazvin University of Medical Science, Qazvin, Iran
***Dr. Mazaher Gholipourmalekabadi* (ORCID: 0000-0001-6287-6831)**

Dr. Mazaher Gholipourmalekabadi
Department of Tissue Engineering & Regenerative Medicine, Faculty of Advanced Technologies in Medicine, Iran University of Medical Sciences, Tehran 1449614535, Iran
Tel: (+98 21) 8862 2755; Fax: (+98 21) 8862 2533
E-mail: mazaher.gholipour@iums.ac.ir; mazaher.gholipour@gmail.com

Abstract

In this study, we synthesized thermo-responsive chitosan (TCTS) hydrogels, and loaded with different concentrations of antimicrobial peptide (AMP) (0, 4, 8 and 16 $\mu g.ml^{-1}$) to fabricate an antibacterial wound dressing against resistant clinical isolates. Physico-chemical properties, release behavior, cytobiocompatibility and antibacterial activity of the AMP-TCTS hydrogels against standard strain and resistant *Acinetobacter baumannii* were fully determined *in vitro*. The TCTS-40% β-glycerolphosphate hydrogels showed a gelation time of 15 min at 37 °C. 80% weight loss at day 35 with no changes in pH value was observed. AMP-TCTS hydrogels showed a burst release of AMP (around 40%) at day 1, and a controlled release up to day 7. A dramatic water uptake was observed at first 4 h, and then continued for 10 h in a steady manner. All the AMP-TCTS hydrogels showed excellent cytobiocompatibility for human fibroblasts. The TCTS showed no antibacterial activity against both standard strain and clinical isolates. All the AMP-TCTS hydrogels had strong antibacterial activity against standard strains, but only 16 $\mu g.ml^{-1}$ showed antibacterial behavior against resistant *A. baumannii*. Our results strongly suggest the 16 $\mu g.ml^{-1}$ AMP-TCTS hydrogel as an excellent antibacterial wound dressing against resistant *A. baumannii*, and now promises to proceed with pre-clinical investigations.

Keywords: chitosan; hydrogel; thermos-responsive; resistant bacteria, post-wound infection; wound dressing;